Certificate of Mailing [37 CFR 1.8(a)]

I hereby certify that this paper and the documents referred to as attached therein are being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandra, VA 22313-1450.

February 2, 2006
Date

Denise Ortega
Name

Denise Ortega
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jan Zavada et al. Group Art Unit: 1643

Serial No.: 09/807,949 Examiner: Christopher H. Yaen

Filed : August 9, 2001

For : MN Gene and Protein

AMENDMENT AND REQUEST FOR
CONTINUED EXAMINATION (RCE)

MAIL STOP RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Amendment concerning the above-identified application is in response to the Advisory Action mailed from the U.S. Patent and Trademark Office (PTO) on January 3, 2006. Applicants respectfully request that the amendments in this response, which were previously submitted in their Amendment

after Final submitted to the PTO on November 9, 2005 but not entered, now be entered in accordance with 37 CFR § 1.114 and with the Manual of Patent Examining Procedure (MPEP) § 706.07(h).

The instant application was filed on August 9, 2001, and is the U.S. national stage application corresponding to PCT Application No. PCT/US99/24879 filed October 22, 1999. Therefore, as the instant application is an international utility application that was filed under 35 U.S.C. 363 after June 8, 1995, and as the last Office action was a Final Office Action closing the prosecution in the application, Applicants respectfully point out that they are entitled under 37 CFR §§ 1.114 (a) and (d) to have a first submission entered and considered on the merits after final rejection:

> If prosecution in an application is closed, an applicant may request continued examination of the application by filing a submission and the fee set forth in § 1.17(e) prior to the earliest of:
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> (a) Payment of the issue fee, unless a petition under § 1.313 is granted;
> (b) Abandonment of the application; or
> (c) The filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. 141, or the commencement of a civil action under 35 U.S.C. 145 or 146, unless the appeal or civil action is terminated. . . .
>
> If an applicant timely files a submission and fee set forth in § 1.17(e), the Office will withdraw the finality of any

Office action and the submission will be entered and considered.

Applicants have enclosed herewith a submission and an authorization to charge the fee of $790 as set forth in 37 CFR § 1.17(e), and note that the finality of the Office Action, mailed from the PTO on September 9, 2005 (hereinafter cited as "Office Action") is thereby automatically withdrawn. Also enclosed is an authorization to charge the fee for a one-month extension of time under 37 CFR § 1.17(a)(1).[1] Should any additional fees be determined to be necessary in connection with this paper, Applicants respectfully request that any such additional fees be charged to Deposit Account No. 12-0615.

SUMMARY OF NOVEMBER 7 INTERVIEW

Applicants would like to thank Examiner Christopher Yaen and his Primary Examiner Sheela Huff for granting an interview on November 7 to the undersigned Attorney for the Applicants and the patent agent with whom she works, Joan

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1. Only a one-month extension fee is due because the Applicants filed their response to the final office action for the instant application within **TWO MONTHS** of the mailing date of the final office action, and the advisory office action was not mailed until after the end of the **THREE MONTH** shortened statutory period. The shortened statutory period then expired on the date the advisory action was mailed, that is, on January 3, 2006, and the extension fee pursuant to 37 CFR 1.136(a) is calculated from the mailing date of the advisory action. The instant

Harland, Ph.D. On Thursday, November 3, Applicants had faxed to the Examiner and his Primary Examiner a Draft Amendment and a graphic (with explanation) to be discussed at the interview.

The Draft Amendment and graphic (with explanation) were discussed at the November 7 interview. Applicants used the graphic to explain why it is that the Zavada et al. 1997 article teaches away from the claimed invention. Applicants explained that Zavada et al. 1997 only provides a method of **not** identifying molecules that bind specifically to MN's cell adhesion site, and not methods of identifying such molecules as claimed in the subject application. Applicants also explained that Zavada et al. 1997 misidentified MN's cell adhesion site as **not** being closely related or identical to the epitope for the M75 monoclonal antibody ("MAb M75").

Applicants further explained that the cell adhesion assay of Zavada et al. 1997 uses a MN fusion protein wherein the non-MN part of the fusion protein,[2] the "GST anchor" of the graphic, was only later discovered to contain a cell binding site of its own. Because of that unrecognized at-the-time fact,

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RCE is being submitted to the PTO within one-month of the advisory action.

2. Zavada et al. 1997 at page 858, col. 2 identified said fusion protein as "MN protein (affinity purified pGEX-3X MN) [citing to Zavada et al., Int. J. Cancer, 54: 268-274 (1993)]" and thereafter referred to said fusion protein as "MN protein."

the assay of Zavada et al. 1997 could actually not determine whether the MN protein is or is not a cell adherence molecule (CAM), because any cell adherence to the fusion protein could have been just to the cell binding site on the non-MN portion of the fusion protein.

Applicants respectfully explained that it would not matter whether NIH3T3 cells or HeLa cells were used in the cell adhesion assay of the 1997 Zavada et al. article, because as the graphic that was faxed on November 3 [that is, the same graphic as within the accompanying Appendix A] schematically illustrates and the explanation accompanying that graphic further elucidates, the cells would always be able to bind to the binding site on the GST anchor, whether or not the binding site on the MN part of the fusion protein was blocked or not.

The Examiner argued that nonetheless that Zavada et al. 1997 anticipated the subject claims because of open language within the claims. Applicants respectfully countered that there is no open language in the claims in regard to the nucleotide sequence that encodes the MN protein/MN polypeptide that comprises MN's cell binding site that is bound to a substrate in the claimed assay; claim 31 at line 30 reads that said nucleotide sequence is "selected from the group **consisting of**: (i) SEQ ID NO: 1 . . ." and nucleotide sequences that are very

closely related to SEQ ID NO: 1. [Emphasis added.] SEQ ID NO: 1 is the cDNA that encodes the MN protein shown in Figure 1.

Applicants respectfully pointed out that said nucleotide sequence [selected from MN's cDNA, SEQ ID NO: 1, and sequences very closely related to SEQ ID NO: 1], that encodes the said MN protein/MN polypeptide which comprises MN's cell binding site, could not by definition include a nucleotide sequence that would encode the MN fusion protein used in Zavada et al. 1997.[3] "Consisting of" is closed, rather than open language. Applicants respectfully submitted that Zavada et al. 1997 cannot anticipate the claimed methods, since the presence of a non-MN cell adhesion site in the non-MN part of the fusion protein used in Zavada et al. 1997 is a very significant material difference between the assay of Zavada et al. 1997 and the assays of the instant invention.

That material difference of the Zavada et al. 1997 assay led exactly in the opposite direction from the

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3. Applicants did explain that ones of the skill in the art, once having the knowledge of the instant application, would realize that one could not use a fusion protein wherein the non-MN portion had a cell binding site in the assays of the instant invention to identify molecules that bind specifically to MN's cell binding site. However, under the doctrine of equivalents, a potential infringer should not be able to avoid the subject claims by using a fusion protein that contains non-MN protein/polypeptide which does not contain a cell binding site, and which would not interfere with cells binding to the cell binding site within the MN portion of the fusion protein.

identification of the nature and location of MN's cell adhesion site, that is disclosed for the first time in the instant application. Because Zavada et al. 1997 used the MN fusion protein that they did, with the then unrecognized non-MN cell adhesion site, Zavada et al. 1997 teaches that the M75 MAb did not bind to MN's cell adhesion site, and consequently that said site is not closely related or identical to the M75 MAb's epitope, and that said site was not within MN's proteoglycan (PG) domain, within which domain M75 MAb's epitope is known to reside. Applicants respectfully described such teachings as those that would lead one of skill in the art directly in the opposite direction away from the actual identity and location of MN's cell binding site.

The Examiner further referred to "open language" in regard to MN's cell binding site, apparently referring to the phrase "said site comprising an amino acid sequence selected from SEQ ID NOS: 10 and 97-106 . . ." [Emphasis added.] Applicants respectfully, but forcefully countered that said "site" is noted in claim 31 to be "within MN's proteoglycan-like domain," and identified that site as closely related or identical to the epitope for MAb M75.

Applicants were respectfully bewildered by how the claim terminology "said site comprising an amino acid sequence selected from SEQ ID NOS: 10 and 97-106" could be interpreted

to include an amino sequence from a non-MN protein/polypeptide, particularly a non-MN protein/polypeptide comprising a non-MN cell binding site. Applicants respectfully reiterated that said site is closely related or identical to the epitope for MAb M75, and that said MAb M75 is specific to the MN protein.

Applicants respectfully pointed out that since MN's cell adhesion site is closely related or identical to the epitope for the MAb M75, and since the MAb M75 is specific for the MN protein, that one of skill in the art, especially in the context of claim 31, wherein said site is identified as within MN's PG domain, would know that said site would not include a non-MN protein/polypeptide sequence, and certainly not an inoperative embodiment wherein said site would include a cell binding site from a non-MN protein/polypeptide. Such an interpretation would not be reasonable in that it would not only be untenable in view of the Specification, the inventive concept underlying the claims, but would also negate the very purpose of the assay, that is, to identify molecules that would bind to **MN's cell adhesion site**, and **not** to **non-MN** cell adhesion sites.

Applicants respectfully concluded that if their arguments and amendments were not found persuasive, that they would appreciate instructions on how to avail themselves of the newly instituted Pre-Appeal Brief Conference procedure. The Examiner and his Primary Examiner responded that the Applicants

should submit their Amendment After Final, and that if necessary, that they would get back to the Applicants with information concerning the Pre-Appeal Brief Conference procedure. Applicants thanked the Examiner and his Primary Examiner for their time and patience in listening to the Applicants' points and explanations, and for their generosity in offering to help the Applicants explore the new Pre-Appeal Brief Conference procedure.